REMARKS

Applicants' representatives thank Examiner Sarada Prasad, Supervisory Examiner Yvonne Eyler and Practice Specialist Paula Hutzell for the courtesy extended during the interview on November 21, 2001. The amendments and remarks herein are made in accordance with our conversations.

Status of the claims

Upon entry of this amendment, claims 26-28, 31-41, 44, 45, 48-81, 83-213, 215-223, 225-238, 240-341, and 343-429 will be pending. Applicants have cancelled claims 1-25, 29, 30, 42, 43, 46, 47, 82, 214, 224, 239 and 342 without prejudice or disclaimer. Applicants reserve the right to file one or more divisional applications directed to inventions not elected in the instant application.

For the Examiner's convenience, a Clean Version of the Entire Set of Pending Claims (including amendments made herein) as allowed for under 37 C.F.R. §1.121(c)(3) is enclosed.

Amendments to the claims

Claims 26, 39, 57, 78, 103, 160, 178, 196, 213, 232, 247, 268, 290, 307, 324 and 341 have been amended in accordance with the discussion during the interview on November 27, 2001.

Claims 29, 30, 42, 43, 46, 47, 214, 224, 239, and 342 have been cancelled as they would be duplicative in light of the amendments made herein. Claim 82 was cancelled because it improperly depended from claim 79. The dependencies of claims 225 and 240 have been amended to account for the amendments made to the claims herein.

Claims 57 and 78 have been amended so there was consistent use of dashes in the claim.

Claims 233-238 have been amended to improve the clarity of the claims.

Claim 273 has been amended so that it is no longer a duplicate of claim 307.

New claims 360-423 directed to polypeptides that modulate leukocyte cell proliferation, differentiation, and survival and new claims 424-429 directed to Neutrokine alpha multimers have been added. Support for new claims 360-423 may be found in the specification as filed, for example, at pages 65-66. Support for new claims 424-429 may be found, for example, on page 2, lines 9 to 17 and pages 80 to 84 of the specification as

filed. No new matter has been added by way of amendment. Applicants respectfully request that these amendments be entered.

Substitute Specification

In accordance with the Examiner's request that Applicants check the specification for minor errors, Applicants provide herewith a Substitute Specification as well as a Version of the Substitute Specification with Markings to Show Changes Made.

The undersigned attorney of record hereby states under 37 C.F.R. §1.125(b)(1) that the substitute specification filed herewith contains no new matter. Each of the amendments to the specification are shown in boldfaced text in the Version of the Specification With Markings to Show Changes Made submitted herewith in which insertions are indicated by underlining and deletions are indicated by strikeout. The amendments either (1) correct grammatical and/or clerical errors; (2) perfect the priority claim; (3) amend the specification to add SEQ ID NOs for sequences disclosed in the specification as filed, (4) harmonize references to the drawings in the specification with the formal drawing labels, or (5) were made and entered previously (i.e., the amendments proposed in the Preliminary Amendment of filed August 14, 2001 have been entered into the Substitute Specification).

With regard to the amendment to the priority claim, Applicants have merely clarified the claim to priority by inserting language describing the priority of U.S. Application 09/255,794. In support of this amendment, Applicants present below the first paragraph of U.S. Application Serial Number 09/255,794 as originally filed and as amended on February 6, 2002:

First paragraph of the 09/255,794 application as originally filed:

> This application is a continuation-in-part of copending application Serial No. 09/005,874, filed January 12, 1998, which is a continuation-in-part of copending applications Serial No. US60/036,100 filed January 14, 1997 and PCT/US96/17957 filed October 25, 1996, each of which is herein incorporated by reference in its entirety.

First paragraph of the 09/255,794 application as amended on February 6, 2002:

> This application is a continuation-in-part of, and claims the benefit of priority under 35 U.S.C. § 120 of, copending U.S. Application Serial No. 09/005,874, filed January 12, 1998, which claims the benefit of priority under 35 U.S.C. § 119(e) of U.S. Provisional Application Serial No.

60/036,100 filed January 14, 1997 and U.S. Application Serial No. 09/005,874 is also a continuation-in-part of, and claims the benefit of priority under 35 U.S.C. § 120 of, International Patent Application No. PCT/US96/17957 filed October 25, 1996. Each of U.S. Application Serial No. 09/005,874, U.S. Provisional Application Serial No. US60/036,100, and International Patent Application No. PCT/US96/17957 is herein incorporated by reference in its entirety.

The February 6, 2002 amendment of the first paragraph of the 09/255,794 specification merely ensures that the priority claim to U.S. Provisional Application Number 60/036,100 is a claim under 35 U.S.C. § 119(e) which was properly identified in the originally filed and executed copy of Declaration for Patent Application (37 C.F.R. §1.63) filed in the 09/255,794 application on May 14, 1999 (enclosed as Exhibit A). Applicants submit herewith a First Supplemental Application Data Sheet also for the purpose of correcting the priority claim. Thus, no new matter has been entered by way of amendment.

Applicants respectfully request that the Substitute Specification submitted herewith be entered.

Replacement Sequence Listing

The Substitute Sequence Listing submitted herewith has been amended to bring the Sequence Listing into compliance with the 37 C.F.R. §1.821- §1.825. Briefly the amendments to the Sequence Listing include: (a) amendment of the header information to correctly identify the present application and the applications to which it claims priority; (b) amendment of the header information preceding primer sequences (SEQ ID NOS: 10-17, 24-26, 31-36 and 39-42) to bring them into the appropriate format; (c) amendments to SEQ ID NO:38 to make the Sequence Listing correctly reflect SEQ ID NO:38 as defined in the originally filed specification, for example at pages 131-133; and (d) to add SEQ ID NOS:39-42 which correspond to sequences disclosed in the originally filed specification at page 342, lines 25-27 and page 343, lines 31 and 32). Each of the amendments is supported by the specification as originally filed and no new matter has been introduced.

Rejections under 35 U.S.C. §112, first paragraph

Claims 26-359 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement and written description. Specifically, the Examiner states that "[t]he specification

does not enable any person skilled in the art to which pertains, or with which it is most nearly connected to make the invention commensurate in scope with these claims." (Paper No. 11, page 5). The Examiner further contends that the claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the invention was filed had possession of the claimed invention." (Paper No. 11, pages 9-10).

Applicants respectfully disagree with the rejections and submit that the claims pending (both prior to, and upon entry of, the present amendment) are fully enabled. Moreover, Applicants respectfully submit that one skilled in the art would reasonably conclude that Applicants had possession of the claimed polypeptides on the filing date of the present application and of the filing date of the earliest priority document to which the present application claims priority.

As discussed during the interview on November 21, 2001, Applicants assert that one skilled in the art, enlightened by the disclosure of the present specification could routinely make the claimed polypeptides, and use the polypeptides (and/or antibodies generated against these polypeptides), for example, to treat or diagnose an autoimmune disease or an immunodeficiency. Additionally, Applicants assert that one skilled in the art could readily envision or recognize a representative number of members of the claimed genera based upon the teachings of the specification as filed, and thus, could reasonably conclude that the inventors had possession of the claimed invention in the specification as filed.

While Applicants maintain that the claims as originally presented were fully enabled and contained only subject matter for which there is written description support in the specification as filed, in the interest of facilitating prosecution of this application, Applicants have amended claims 26, 39, 57, 78, 103, 160, 178, 196, 213, 232, 247, 268, 290, 307, 324 and 341, in accordance with the discussions during the interview on November 21, 2001.

Applicants believe that in view of the discussion above and at the interview of November 21, 2001, and in view of the amendments made herein, this rejection has been obviated or overcome. Applicants respectfully request that this rejection under 35 U.S.C. §112 be reconsidered and withdrawn.

Availability of Deposited Plasmids

The Examiner has indicated concern over the availability of the deposited biological material. In order to allay these concerns, Applicants' representative makes the following statement for the record.

The undersigned attorney of record in the instant application hereby states that the deposited plasmid HNEDU15, accorded ATCC Deposit Number 97768, will be irrevocably and without restriction, except for the limitations allowed by 37 C.F.R. § 1.808(b), released to the public upon the issuance of a patent containing claims reciting said plasmid for the instant application.

Applicants believe that all the requirements of 37 C.F.R. §§ 1.801-809 have been met with respect to the deposited plasmid recited in the claims.

Rejections under 35 U.S.C. §102(e)

Claims 26-359 have been rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,297,367 to Tribouley et al. issued October 2, 2001 and claiming priority back to December 30, 1997. This rejection is improper due to the fact that the instant application has an effective filing date of October 25, 1996, which is more than one year prior to the December 30, 1997 priority filing of U.S. Patent No. 6,297,367. In light of the fact that the priority date of U.S. Patent No. 6,297,367, is later than the priority date of the instant application, U.S. Patent No. 6,297,367 is not prior art under 35 U.S.C. §102(e). Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. §102(e) be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks of the present Amendment be entered and made of record in the present application.

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance. An early Notice of Allowance is earnestly solicited. If in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425.

Respectfully submitted,

Date: May 3, 2002

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KKH/MS/vsr

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Yu et al.
Application No.: 09/507,968
Filed: February 22, 2000
For: **Neutrokine-alpha and Neutrokine-alpha Splice Variant**

Art Unit: 1646
Examiner: S. Prasad
Atty Docket No.: PF343P3

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments are shown in bold with insertions indicated with underlining and deletions indicated by strikeout.

In the Specification:

The specification has been replaced with the Substitute Specification filed herewith.

In the Sequence Listing:

The Sequence Listing been replaced with the Substitute Sequence Listing submitted herewith.

In the Claims:

Claims 1-25, 29, 30, 42, 43, 46, 47, 82, 214, 224, 239 and 342 have been cancelled without prejudice or disclaimer.

Claims 360-429 have been added.

Please replace each of claims 26, 39, 57, 78, 103, 160, 178, 196, 213, 225, 232-238, 240, 247, 268, 273, 290, 307, 324 and 341 with the corresponding amended claim below:

26. (Amended) An isolated protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues 1 to 285 of SEQ ID NO:2; **and**

~~**(b) the amino acid sequence of amino acid residues 1 to 46 of SEQ ID NO:2;**~~

~~**(c) the amino acid sequence of amino acid residues 47 to 72 of SEQ ID NO:2; and**~~

(b)~~**(d)**~~ the amino acid sequence of amino acid residues 73 to 285 of SEQ ID NO:2.

39. (Amended) An isolated protein comprising a first amino acid sequence that is 90% or more identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues 1 to 285 of SEQ ID NO:2; **and**

~~**(b) the amino acid sequence of amino acid residues 1 to 46 of SEQ ID NO:2;**~~

~~**(c) the amino acid sequence of amino acid residues 47 to 72 of SEQ ID NO:2; and**~~

(b)~~**(d)**~~ the amino acid sequence of amino acid residues 73 to 285 of SEQ ID NO:2~~.~~**;**

wherein said protein modulates leukocyte proliferation, differentiation or survival.

57. (Amended) An isolated protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of **274-284** ~~**274 to 284**~~; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284;

wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

78. (Amended) An isolated protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues n to 285 of SEQ ID NO:2, where n is an integer in the range of 2-190;

(b) the amino acid sequence of amino acid residues 1 to m of SEQ ID NO:2, where m is an integer in the range of **274-284** ~~**274 to 284**~~; and

(c) the amino acid sequence of amino acid residues n to m of SEQ ID NO:2, where n is an integer in the range of 2-190 and m is an integer in the range of 274-284; and

wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

103. (Amended) An isolated protein comprising the amino acid sequence of amino acid residues 191-285 of SEQ ID NO:2, wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

160. (Amended) An isolated protein **consisting of an amino acid sequence** that is 90% or more identical to **the** ~~**an**~~ amino acid sequence ~~**consisting**~~ of amino acid residues 134-285 of SEQ ID NO:2, wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

178. (Amended) An isolated protein **comprising an amino acid sequence** that is 90% or more identical to ~~**an**~~ **the** amino acid sequence ~~**comprising**~~ **of** amino acid residues 134-285 of SEQ ID NO:2, wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

196. (Amended) An isolated protein comprising a fragment of the polypeptide of SEQ ID NO:2, wherein said fragment modulates leukocyte proliferation, ~~**or**~~ differentiation **or survival**.

213. (Amended) An isolated protein comprising an amino acid sequence of at least ~~**9**~~ **30** contiguous amino acid residues of SEQ ID NO:2 wherein said protein ~~**specifically binds to an antibody that specifically binds the protein of SEQ ID NO:2**~~ **modulates leukocyte proliferation, differentiation or survival**.

225. (Amended) The protein of claim ~~**224**~~ **213** wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

232. (Amended) An isolated protein ~~which comprises an~~ **consisting of a fragment of SEQ ID NO:2 fused to a heterologous amino acid sequence, wherein said fragment comprises an** amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of amino acid residues 115 to 147 of SEQ ID NO:2;

(b) the amino acid sequence of amino acid residues 150 to 163 of SEQ ID NO:2;

(c) the amino acid sequence of amino acid residues 171 to 194 of SEQ ID NO:2;

(d) the amino acid sequence of amino acid residues 223 to 247 of SEQ ID NO:2; and

(e) the amino acid sequence of amino acid residues 271 to 278 of SEQ ID NO:2.

~~wherein said protein specifically binds to an antibody that specifically binds the polypeptide of SEQ ID NO:2~~.

233. (Amended) The protein of claim 232 ~~which~~ **wherein said fragment** comprises amino acid sequence (a).

234. (Amended) The protein of claim 232 ~~which~~ **wherein said fragment** comprises amino acid sequence (b).

235. (Amended) The protein of claim 232 ~~which~~ **wherein said fragment** comprises amino acid sequence (c).

236. (Amended) The protein of claim 235 ~~which~~ **wherein said fragment** also comprises amino acid sequence (d).

237. (Amended) The protein of claim 232 ~~which~~ **wherein said fragment** comprises amino acid sequence (d).

238. (Amended) The protein of claim 232 ~~which~~ **wherein said fragment** comprises amino acid sequence (e).

240. (Amended) The protein of claim ~~239~~ **232** wherein the heterologous amino acid sequence is the amino acid sequence of an immunoglobulin Fc domain.

247. (Amended) An isolated protein comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of an amino-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino-terminal deletion protein mutant excludes up to 190 amino acid residues from the amino terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768;

(b) the amino acid sequence of a carboxy-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said carboxy-terminal deletion protein mutant excludes up to 11 amino acid residues from the carboxy terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768; and

(c) the amino acid sequence of an amino- and carboxy-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino- and carboxy-terminal deletion protein mutant excludes up to 190 amino acid residues from the amino terminus and up to 11 amino acid residues from the carboxy terminus of said said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768;

wherein said protein ~~specifically binds an antibody that specifically binds the polypeptide encoded by the cDNA clone contained in ATCC Deposit Number 97768~~ **modulates leukocyte proliferation, differentiation or survival**.

268. (Amended) An isolated protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of an amino-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino-terminal deletion protein mutant excludes up to 190 amino acid residues from the amino terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768;

(b) the amino acid sequence of a carboxy-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said carboxy-terminal deletion protein mutant excludes up to 11 amino acid residues from the carboxy terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768; and

(c) the amino acid sequence of an amino- and carboxy-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino- and carboxy-terminal deletion protein mutant excludes up to 190 amino acid residues from the amino terminus and up to 11 amino acid residues from the carboxy terminus of said said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768;

wherein said protein ~~**specifically binds an antibody that specifically binds the polypeptide encoded by the cDNA clone contained in ATCC Deposit Number 97768**~~ **modulates leukocyte proliferation, differentiation or survival**.

273. (Amended) The protein of claim 269 which excludes **71** ~~**133**~~ amino acid residues from the amino terminus of the full length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768.

290. (Amended) An isolated protein comprising a first amino acid sequence that is 95% or more identical to a second amino acid sequence consisting of the amino acid sequence of an amino-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino-terminal deletion protein mutant excludes up to 133 amino acid residues from the amino terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, and wherein said ~~isolated protein specifically binds an antibody that specifically binds the protein of SEQ ID NO:2~~ **protein modulates leukocyte proliferation, differentiation or survival**.

307. (Amended) An isolated protein consisting of a first amino acid sequence that is 95% or more identical to a second amino acid sequence consisting of the amino acid sequence of an amino-terminal deletion protein mutant of the full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said amino-terminal deletion protein mutant excludes up to 133 amino acid residues from the amino terminus of said full-length protein encoded by the cDNA clone contained in ATCC Deposit Number 97768, and wherein said ~~isolated protein specifically binds an antibody that specifically binds the protein of SEQ ID NO:2~~ **protein modulates leukocyte proliferation, differentiation or survival**.

324. An isolated protein comprising a fragment of the polypeptide encoded by the cDNA clone contained in ATCC Deposit Number 97768, wherein said fragment modulates leukocyte proliferation**,** ~~or~~ differentiation **or survival**.

341. (Amended) An isolated protein comprising an amino acid sequence of at least ~~9~~ **30** contiguous amino acid residues of the polypeptide encoded by the cDNA clone contained in ATCC Deposit Number 97768 wherein said protein ~~specifically binds an antibody that specifically binds the polypeptide encoded by the cDNA clone contained in ATCC Deposit Number 97768~~ **modulates leukocyte proliferation, differentiation or survival**.